and a mixture thereof.

According to the citation,

> In general, drug administration via the skin is divided into two categories: 1) transdermal administration and 2) intradermal administration. Transdermal administration involves transport through the skin and into the blood stream to treat systemic diseases. One the other hand, intradermal administration is intended to impart a cutaneous effect, while keeping the pharmocological effects of the drug localized to the intracutaneous regions of drug penetration and deposition. Ideally, intradermal absorption occurs with little or no systemic absorption or accumulation.

See column 1, lines 39-49. Nothing in this general statement provides motivation in any direction. Merely the two types of administrations via the skin are described along with their sites of actions.

Moreover, Fisher also teaches that

> The controlled release of drugs into the epidermis or dermis, with the assurance that the drug remains primarily localized and does not enter the blood stream in significant amounts requires innovative approaches. Further complicating the matter, the behavior of a penetration agent is strongly dependant on the drug. That is, a given penetration agent does not necessarily increase the penetration of all drugs. (Internal citations omitted.)

See column 2, lines 29-38. Thus, Fisher clearly teaches that there are challenges with targeting the epidermis or dermis, including the requirement of innovative approaches to assure that the drug remain primarily localized. Also taught is that the behavior of the penetrating agent is strongly dependent on the drug, whereby there is an uncertainty even after the selection of a penetrating agent whether it would increase the penetration of a given drug.

This background information clearly teaches to one of ordinary skill in the art that generalizations even from the combination actually taught in Fisher, i.e., local anesthetic, and an aloe composition and/or a triglyceride, should be made with caution.

Additionally, this reference is completely silent on any compound, e.g., hyaluronic acid, etc., recited in the present claims, or their behavior. And as such, it provides no teaching whatsoever in any direction regarding the administration routes thereof, or any relevant material to the present invention.

The Office Action alleges that one would chose the route of administration to receive

the expected benefit, ... keeping the pharmacological effects of the drug localized ... to provide the best route of administration.

However, Falk teaches that the mode of administration taught therein, which is topical administration transdermally is "best targeting the epidermis and subsequently remaining there for a prolonged period of time." See the bottom of column 6 at lines 64-68. No reason is provided thereby to one of ordinary skill in the art to change this disclosed best administration route to target the epidermis to something else, to achieve the same goals (localized targeting with the drug remaining at the targeted site), i.e., nonsystemic acting, not acting essentially through the blood. See column 7, lines 27-30.

Fischer only generally refers to intradermal administration of drugs and does not at all mention hyaluronic acid in crosslinked form. Consequently, for even this reason alone, the combination of Falk, Sakurai and Fischer is improper. Neither Falk nor Sakurai even remotely suggests any problems with the topical administration of hyaluronic acid, e.g., in crosslinked form. To the contrary, Falk specifically states that it is the "best targeting the epidermis." Thus, one of ordinary skill in the art would not have been motivated to consider routes of administration for hyaluronic acid in crosslinked form other than topical administration, as proposed by Falk and Sakurai.

In particular, however, a combination of Falk, Sakurai and Fischer also leads away from the subject matter of the present application. On the one hand, Falk does not disclose hyaluronic acid as an active ingredient, but only as a penetration agent for allowing an inhibitor of prostaglandin synthesis to penetrate the skin. On the other hand, Fischer does not at all teach intradermal application of drugs, as alleged by the Examiner. Fischer addresses the problem of drugs which are per se not capable of penetrating the skin and mentions transdermal and intradermal administration as a known solution to this problem. However, the citation itself does not at all suggest intradermal administration of drugs, but teaches topical application of a combination of the drug in question and a penetration agent, since topical application provides a number of advantages over other routes of administration (cf. column 1, lines 11-18, of Fischer).

In view of the above, a person skilled in the art would not have been motivated to intradermally administer hyaluronic acid in crosslinked form for treating inflammatory skin or mucous membrane diseases. As such, the combination of Falk, Sakurai and Fischer does not render the claimed subject matter obvious.

Claims 5 and 6 are rejected as allegedly unpatentable over Flak in view of Sakurai and Fischer and in further view of Wilkinson.

Wilkinson does not cure the deficiencies of the primary references. Thus, for at least the reason discussed above, these claims are also patentable.

Reconsideration is respectfully requested.

Election/Restriction

As to the various election of species requirements, which is the reason for all the withdrawn claims, in accordance with M.P.E.P. 803.02, the Examiner is reminded that, should no prior art be found which renders the invention of the elected species unpatentable (which is the case as established above), the search of the remainder of the generic claim(s) should be continued in the same application.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. See MPEP 803.02 in accord.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Csaba Henter/

Csaba Henter, Reg. No. 50,908
Attorney for Applicants

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1
2200 Clarendon Boulevard, Suite 1400
Arlington, VA 22201
Telephone: 703-243-6333
Facsimile: 703-243-6410
Attorney Docket No.: WEICKM-0061

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